	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	0	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex) and (raloxifen or droloxifen or centchroman)	USPAT	2000/10/25 12:12			0
2	BRS	L2	201	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex) or (raloxifen or droloxifen or centchroman)	USPAT	2000/10/25 12:20			0
3	BRS	L3	21	2 and bone near4 dens$	USPAT	2000/10/25 12:14		Truncation Overflow. Return string from Server is: 5`43221`5	1
4	BRS	L4	4	2 and osteopen$	USPAT	2000/10/25 12:14			0
5	BRS	L5	484	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex) or (raloxifen$2 or droloxifen$2 or centchroman)	USPAT	2000/10/25 12:24			0
6	BRS	L6	138	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex)	USPAT	2000/10/25 12:22			0
7	BRS	L7	545	lhrh near3 (analog$ or agonist$2 or antagonist$2)	USPAT	2000/10/25 12:24			0
8	BRS	L8	616	(6 or 7)	USPAT	2000/10/25 12:24			0
9	BRS	L9	19	8 and (raloxifen$2 or droloxifen$2 or centchroman)	USPAT	2000/10/25 12:25			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
10	BRS	L10	8	9 and (osteopen$ or bone near4 loss or bone near4 densit$)	USPAT	2000/10/25 12:34		Truncation Overflow. Return string from Server is: 5`0`0`OST	1
11	BRS	L11	9	9 and osteopor$	USPAT	2000/10/25 12:41			0
12	IS&R	L12	1	("5457117").PN.	USPAT	2000/10/25 12:41			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	0	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex) and (raloxifen or droloxifen or centchroman)	USPAT	2000/10/25 12:12			0
2	BRS	L2	201	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex) or (raloxifen or droloxifen or centchroman)	USPAT	2000/10/25 12:20			0
3	BRS	L3	21	2 and bone near4 dens$	USPAT	2000/10/25 12:14		Truncation Overflow. Return string from Server is: 5`43221`5	1
4	BRS	L4	4	2 and osteopen$	USPAT	2000/10/25 12:14			0
5	BRS	L5	484	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex) or (raloxifen$2 or droloxifen$2 or centchroman)	USPAT	2000/10/25 12:24			0
6	BRS	L6	138	(leuprorelin or cetrorelix or bulerelin or antide or ramorelix or zoladex)	USPAT	2000/10/25 12:22			0
7	BRS	L7	545	lhrh near3 (analog$ or agonist$2 or antagonist$2)	USPAT	2000/10/25 12:43			0
8	BRS	L8	616	(6 or 7)	USPAT	2000/10/25 12:24			0
9	BRS	L9	19	8 and (raloxifen$2 or droloxifen$2 or centchroman)	USPAT	2000/10/25 12:25			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
10	BRS	L10	8	9 and (osteopen$ or bone near4 loss or bone near4 densit$)	USPAT	2000/10/25 12:34		Truncation Overflow. Return string from Server is: 5`0`0`OST	1
11	BRS	L11	9	9 and osteopor$	USPAT	2000/10/25 12:41			0
12	IS&R	L12	1	("5457117").PN.	USPAT	2000/10/25 12:41			0
13	BRS	L13	75	lhrh near3 (analog$ or agonist$2 or antagonist$2) and (antiestrogen$2 or anti adj estrogen$2 or anti adj oestrogen$2)	USPAT	2000/10/25 12:45			0
14	BRS	L14	34	13 and (osteopen$ or osteoporo$)	USPAT	2000/10/25 12:46			0

(FILE 'HOME' ENTERED AT 13:21:01 ON 25 OCT 2000)

FILE 'CAPLUS, MEDLINE, BIOSIS' ENTERED AT 13:21:21 ON 25 OCT 2000
L1 4 S (LEUPRORELIN? OR CETRORELIX OR BULERELIN? OR ANTIDE# OR RAMOR
L2 0 S L1 AND (OSTEOPORO? OR OSTEOPEN? OR BONE(4A)(LOSS? OR REDUC?))
L3 133 S (LHRH OR LUTEINIZING (2A)HORMONE (2A) RELEASING (2A) HORMONE#
L4 2 S L3 AND (OSTEOPORO? OR OSTEOPEN? OR BONE(4A)(LOSS? OR REDUC?)
L5 2 DUP REM L4 (0 DUPLICATES REMOVED)

```
FILE 'CAPLUS' ENTERED AT 13:21:21 ON 25 OCT 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2000 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 13:21:21 ON 25 OCT 2000

FILE 'BIOSIS' ENTERED AT 13:21:21 ON 25 OCT 2000
COPYRIGHT (C) 2000 BIOSIS(R)

=> s (leuprorelin? or cetrorelix or bulerelin? or antide# or ramorelix or
zoladex) and (raloxifen? or droloxifen? or centchroman)

L1          4 (LEUPRORELIN? OR CETRORELIX OR BULERELIN? OR ANTIDE# OR
RAMORELI
              X OR ZOLADEX) AND (RALOXIFEN? OR DROLOXIFEN? OR CENTCHROMAN)

=> s l1 and (osteoporo? or osteopen? or bone(4a)(loss? or reduc?))

L2          0 L1 AND (OSTEOPORO? OR OSTEOPEN? OR BONE(4A)(LOSS? OR REDUC?))

=> s (lhrh or luteinizing (2a)hormone (2a) releasing (2a)
hormone#)(p)(analog? or agonist# or antagonist#) and (antiestrogen# or
anti(2a)estrogen# or anti(2a)oestrogen# or antioestrogen#)

L3        133 (LHRH OR LUTEINIZING (2A) HORMONE (2A) RELEASING (2A)
HORMONE#)(
                P)(ANALOG? OR AGONIST# OR ANTAGONIST#) AND (ANTIESTROGEN# OR
                ANTI(2A) ESTROGEN# OR ANTI(2A) OESTROGEN# OR ANTIOESTROGEN#)

=> s l3 and (osteoporo? or osteopen? or bone(4a)(loss? or reduc?))

L4          2 L3 AND (OSTEOPORO? OR OSTEOPEN? OR BONE(4A)(LOSS? OR REDUC?))

=> dup rem l4

PROCESSING COMPLETED FOR L4
L5          2 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l5 abs ibib kwic 1-2


L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2000 ACS
AB   Androst-5-ene-3.beta.,17.beta.-diol is used to treat or reduce the
     likelihood of acquiring osteoporosis or menopausal symptoms, or
     other diseases affected by estrogen receptor activity, and for conditions
     which respond well to DHEA treatment, but where a higher ratio of
     estrogenic to androgenic effects is desired.  Combination therapies are
     included, as are kits and pharmaceutical compns. for providing the active
     ingredients of claimed methods and combinations.
ACCESSION NUMBER:        1999:795632  CAPLUS
DOCUMENT NUMBER:         132:19230
TITLE:                   Pharmaceutical compositions and uses for
                         androst-5-ene-3.beta.,17.beta.-diol in treating
                       osteoporosis, menopausal symptoms, or other
```

diseases affected by estrogen receptor activity

INVENTOR(S): Labrie, Fernand

PATENT ASSIGNEE(S): Endorecherche, Inc., Can.

SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9963973	A2	19991216	WO 1999-CA537	19990610
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941274	A1	19991230	AU 1999-41274	19990610
PRIORITY APPLN. INFO.:			US 1998-96286	19980611
			WO 1999-CA537	19990610

TI Pharmaceutical compositions and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity

AB Androst-5-ene-3.beta.,17.beta.-diol is used to treat or reduce the likelihood of acquiring **osteoporosis** or menopausal symptoms, or other diseases affected by estrogen receptor activity, and for conditions which respond well to DHEA treatment, but where a higher ratio of estrogenic to androgenic effects is desired. Combination therapies are included, as are kits and pharmaceutical compns. for providing the active ingredients of claimed methods and combinations.

ST androstenediol pharmaceutical compns uses; **osteoporosis** androstenediol treatment; menopausal symptoms androstenediol treatment; estrogen receptor related diseases androstenediol treatment

IT Androgens
Estrogens
Progestogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androst-5-ene-3.beta.,17.beta.-diol in combination with other steroids
or drugs for treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antiestrogens**; androst-5-ene-3.beta.,17.beta.-diol in combination with other steroids or drugs for treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Muscle, disease
Skin, disease
Vagina
(atrophy; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Sexual behavior
(decreased libido; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor

activity)

IT Skin
(dryness; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Uterus, disease
(endometriosis; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Reproductive tract
(hypogonadism; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Bladder
(incontinence; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Ovary, neoplasm
Uterus, neoplasm
(inhibitors; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Memory, biological
(loss; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Antitumor agents
(mammary gland; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Mammary gland
(neoplasm, inhibitors; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Antitumor agents
(ovary; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Anti-Alzheimer's agents
Antiobesity agents
Atherosclerosis
Cardiovascular agents
Cognition enhancers
Drug delivery systems
Fatigue, biological
Menopause
Osteoporosis
(pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Drug delivery systems
(prodrugs, for androst-5-ene-3.beta.,17.beta.-diol; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Drug delivery systems

(transdermal patch; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT Antitumor agents
(uterus; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT 9034-40-6, **LHRH**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**agonists** or **antagonists**; androst-5-ene-3.beta.,17.beta.-diol in combination with other steroids or drugs for treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT 53-43-0, Dehydroepiandrosterone 651-48-9, Dehydroepiandrosterone sulfate
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androst-5-ene-3.beta.,17.beta.-diol in combination with other steroids or drugs for treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT 9015-81-0, 17.beta.-Hydroxy steroid dehydrogenase 9039-48-9, Aromatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; androst-5-ene-3.beta.,17.beta.-diol in combination with other steroids or drugs for treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT 521-17-5, Androst-5-ene-3.beta.,17.beta.-diol
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

IT 9004-10-8, Insulin, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(resistance; pharmaceutical compns. and uses for androst-5-ene-3.beta.,17.beta.-diol in treating **osteoporosis**, menopausal symptoms, or other diseases affected by estrogen receptor activity)

L5 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2000 BIOSIS

AB In young women chronic use of **luteinizing hormone releasing hormone** (**LHRH**) **agonists** such as buserelin to treat endometriosis leads to estrogen-deficiency **bone loss**. Tamoxifen citrate is an estrogen **agonist/antagonist** which protects the skeleton from **osteopenia** when ovarian hormones are depleted. The present study ws undertaken to determine whether tamoxifen citrate (20 mg/kg body wt/week s.c.) could prevent the **osteopenic** effect of buserelin (25 .mu.g/kg body wt/day s.c.). Four groups of rats with 45Ca-labelled bones were studied for 4 weeks: group A - placebo controls; group B - buserelin; Group C-tamoxifen; group D - buserelin + tamoxifen. Bone resorption was monitored by measuring the urinary excretion of 45Ca and hydroxyproline. Interestingly buserelin lowered both blood 17.beta.-estradiol values and uterine weights in the presence and absence of tamoxifen. However, tamoxifen slowed bone breakdown and inhibited the bone-thinning effects of buserelin. Total body calcium values (mg; means .+-. S.D.) were: 2227 .+-. 137; 1926 .+-. 124; 2233 .+-. 94 and 2268 .+-. 168, in groups A to D respectively. **Osteopenia** was thus present only in group B ($P < 0.001$). Because tamoxifen inhibits estrogen-deficiency **bone loss** in buserelin-treated rats without depressing the hypoestrogenic actions of this **LHRH-agonist**, we suggest that use of tamoxifen to protect the skeleton during **LHRH-agonist** therapy in young women should be

explored. Tamoxifen citrate might also help to prevent postmenopausal **osteoporosis**.

ACCESSION NUMBER: 1992:473020 BIOSIS
DOCUMENT NUMBER: BA94:104395
TITLE: TAMOXIFEN IN THE RAT PREVENTS ESTROGEN-DEFICIENCY **BONE LOSS** ELICITED WITH THE **LHRH AGONIST** BUSERELIN.
AUTHOR(S): GOULDING A; GOLD E; FENG W
CORPORATE SOURCE: DEP. MEDICINE, UNIVERSITY OTAGO MEDICAL SCHOOL, P.O. BOX 913, DUNEDIN, NEW ZEALAND.
SOURCE: BONE MINER, (1992) 18 (2), 143-152.
CODEN: BOMIET. ISSN: 0169-6009.
FILE SEGMENT: BA; OLD
LANGUAGE: English

TI TAMOXIFEN IN THE RAT PREVENTS ESTROGEN-DEFICIENCY **BONE LOSS** ELICITED WITH THE **LHRH AGONIST** BUSERELIN.

AB In young women chronic use of **luteinizing hormone releasing hormone (LHRH) agonists** such as buserelin to treat endometriosis leads to estrogen-deficiency **bone loss**. Tamoxifen citrate is an estrogen **agonist/antagonist** which protects the skeleton from **osteopenia** when ovarian hormones are depleted. The present study ws undertaken to determine whether tamoxifen citrate (20 mg/kg body wt/week s.c.) could prevent the **osteopenic** effect of buserelin (25 .mu.g/kg body wt/day s.c.). Four groups of rats with 45Ca-labelled bones were studied for 4 weeks:. . . were: 2227 .+-. 137; 1926 .+-. 124; 2233 .+-. 94 and 2268 .+-. 163, in groups A to D respectively. **Osteopenia** was thus present only in group B ($P < 0.001$). Because tamoxifen inhibits estrogen-deficiency **bone loss** in buserelin-treated rats without depressing the hypoestrogenic actions of this **LHRH-agonist**, we suggest that use of tamoxifen to protect the skeleton during **LHRH-agonist** therapy in young women should be explored. Tamoxifen citrate might also help to prevent postmenopausal **osteoporosis**.

IT Miscellaneous Descriptors
HUMAN ANIMAL MODEL HORMONE-DRUG PHARMACODYNAMICS **ANTIESTROGEN OSTEOPOROSIS** SIDE EFFECT ATTENUATION ENDOMETRIOSIS

=> s ep 897721/pn

L1 1 EP 897721/PN
(EP897721/PN)

no US equivalents

=> d l1 fam 1

L1 ANSWER 1 OF 1 INPADOC COPYRIGHT 2000 EPO

PATENT FAMILY INFORMATION
AN 27289107 INPADOC

PRAI			AI		
US 1997-56202	P	19970821	AU 1998-89128	A	19980818
			EP 1998-306551	A	19980818
			WO 1998-US17116	A	19980818
WO 1998-US17116	W	19980818	AU 1998-89128	A	19980818

AI			PI		
AU 1998-89128	A	19980818	AU 9889128	A1	19990308
EP 1998-306551	A	19980818	EP 897721	A2	19990224
			EP 897721	A3	19990303
WO 1998-US17116	A	19980818	WO 9908677	A1	19990225

2 priorities, 3 applications, 4 publications

L1 ANSWER 1 OF 1 INPADOC COPYRIGHT 2000 EPO

LEVEL 1
AN 27289107 INPADOC EW 199908 UP 20000313 UW 200010
TI BENZO(B)THIOPHENE DERIVATIVES FOR INHIBITING DETRIMENTAL SIDE-EFFECTS
DUE
TO GNRH OR GNRH AGONIST ADMINISTRATION
IN BRYANT, HENRY UHLMAN; CULLINAN, GEORGE JOSEPH; DODGE, JEFFREY ALAN
INS BRYANT HENRY UHLMAN; CULLINAN GEORGE JOSEPH; DODGE JEFFREY ALAN
INA US; US; US
PA ELI LILLY AND COMPANY
PAS LILLY CO ELI
PAA US
TL English; French; German
LA English
DT Patent
PIT EPA2 PUBL. OF APPLICATION WITHOUT SEARCH REPORT
PI **EP 897721 A2 19990224**
DS R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU NL PT SE
AI EP 1998-306551 A 19980818
PRAI US 1997-56202 P 19970821
OSDW 99-134460

LEVEL 2
AN 27289107 INPADOC EW 199908 UP 20000313 UW 200010
PA ELI LILLY AND COMPANY
PAS LILLY CO ELI
DT Patent
PIT EPA3 PUBL. OF SEARCH REPORT
PI **EP 897721 A3 19990303**
DS R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AI EP 1998-306551 A 19980818
PRAI US 1997-56202 P 19970821
OSCA 130:200940